

**REMARKS**

First, this response is intended to provoke an interference between this patent application and U.S. Patent 6,285,027 B1, issued on September 4, 2001. This copying of claims in the '027 patent is timely since these claims are submitted within one year of the issue date of the '027 patent.

For purposes hereinafter, the following is a list of proposed counts and supporting documentation listing the specification locations at which there is material supporting the claims corresponding to the counts in both this application as related to claim 1 of the '027 patent (now claim 115 in this application) and counts 2, 3 and 4, which are claims 66, 80 and 99. There are many other claims that correspond to the proposed counts. Also, the proposed counts are merely illustrative, and there are many additional counts which can be added as this interference proceeds. Additionally, reference to the specifications in the respective application and patent is merely illustrative, and there are additional supporting citations allowing each of the parties to be able to make these proposed counts as well as many others that may be added hereinafter.

In accordance with 37 CFR 1.607, the applicant herein requests interference with US Patent 6,285,027.

- (1) Identifying the patent: US Patent 6,285,027 issued September 4, 2001.
- (2) Presenting a proposed count: Listed hereinafter are four proposed counts.

**Count 1.**

A method of effecting mass analysis on an ion stream, the method comprising:

- (a) passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass-to-charge ratio;
- (b) subjecting the parent ions to collision-induced dissociation to generate fragment ions;
- (c) trapping the fragment ions and any remaining parent ions;

(d) periodically releasing pulses of the trapped ions into a time of flight instrument to detect ions with a second mass-to-charge ratio; and

(e) providing a delay between the release of the pulses of trapped ions and initiation of push-pull pulses in the time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio.

Count 2.

An Apparatus for analyzing chemical species comprising;

- (a) at least one vacuum pumping stage;
- (b) an ion source for producing ions from a sample substance;
- (c) at least one multipole ion guide located in at least one of said vacuum

pumping stages;

(d) a Time-Of-Flight mass to charge analyzer;

(e) means for delivering said ions from said at least one multipole ion guide;

(f) means for applying electrical potentials to at least one multipole ion guide to select parent ions from said ions having a desired mass to charge ratio;

(g) means for applying electrical potentials to at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions;

(h) means to trap said fragment ions and any remaining said parent ions in said at least one multipole ion guide;

(i) means to periodically release pulses of said trapped ions into said Time-Of-Flight mass to charge analyzer to detect said fragment ions with a second mass to charge ratio;

(j) means for providing a delay between the release of the said pulses of said trapped ions and initiation of pulses in the Time-of-Flight mass to charge analyzer; and

(k) means to adjust the delay to improve the duty cycle efficiency of said fragment ions with said second mass to charge ratio.

Count 3.

An apparatus for analyzing chemical species comprising;

- (a) at least one vacuum pumping stage;
- (b) an ion source for producing ions from a sample substance;
- (c) at least two multipole ion guides located in at least one of said vacuum pumping stages;
- (d) a Time-Of-Flight mass to charge analyzer;
- (e) means for delivering said ions from said ion source into at least one multipole ion guide;
- (f) means for applying electrical potentials to a first multipole ion guide to select at least one range of mass to charge values or parent ions; and
- (g) means for applying electrical potentials to at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions in a second multipole ion guide;

Count 4.

A method of effecting mass analysis on an ion stream, the method comprising;

- (a) passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass to charge ratio;
- (b) subjecting the parent ions to collision induced dissociation to generate fragment ions;
- (c) trapping the fragment ions and any remaining parent ions;
- (d) periodically releasing pulses of the trapped ions into a Time-Of-Flight instrument to detect ions with a second mass to charge ratio; and
- (e) providing a delay between the release of the pulses of trapped ions and initiation of pulses in the time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass to charge ratio.

Proposed counts 2, 3 and 4 are taken from new pending claims 66, 80 and 99. Claim 115 is a copy of claim 1 of the '027 patent and claims 116-120 are identical to claims 2-6 of the '027 patent.

(3) Identifying at least one claim in the patent corresponding to the proposed count:

Claim 1 of the '027 patent corresponds to all four of the proposed counts and is identical to count one.

(4) Presenting at least one claim corresponding to the proposed count or identifying at least one claim already pending in its application that corresponds to the proposed count:

Claim 115 corresponds to proposed count 1.

Claim 1 of the '027 patent also corresponds to counts 2-4.

Listed below are each of the counts and the respective specification material in the corresponding patent or pending application corresponding to the proposed counts.

For ease of reference, in Table 1 below, Column I shows claim 115(a)-(e). Column II shows the support at the column and line of U.S. Patent Number 6,011,259. This is followed, in parenthesis, by the location at the page and line of the pending application 09/901,428.

Count I

	Claims 1(a)-(e) of U.S. Patent No. 6,285,027	Support in Pending U.S. Application No. 09/901,428
1	<p>A method of effecting mass analysis on an ion stream, the method comprising:</p> <p>(a) "passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass-to-charge ratio";</p>	<p>Column 8, lines 55-57 of the '259 patent (p.15, lines 17-19 of the application).</p>
	<p>(b) Subjecting the parent ions to collision-induced dissociation to generate fragment ions</p>	<p>Column 8, lines 1-7 of the '259 patent (p.14, lines 4-7 of the application).</p>
✓	<p>(c) <u>Trapping the fragment ions and any remaining parent ions</u></p>	<p>Column 2, lines 50-54 (p.3, lines 21-23 - p. 4, line 1 of the application).</p>
✓	<p>(d) Periodically releasing pulses of trapped ions into a time of flight instrument to detect ions with a second mass-to-charge ratio</p>	<p>Column 8, lines 31-35 of the '259 patent (p.14, lines 2-7 of the application). <i>no mention of periodically releasing pulses of trapped ions with a second mass-to-charge ratio</i></p>
	<p>(e) providing a delay between the release of the pulses of trapped ions and initiation of push-pull pulses in the time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio</p>	<p>Column 7, lines 36-43 (p.13 lines 5-12 of the application). <i>no delay mentioned</i>          Column 12, lines 10-14 (p.22, lines 18-19 of the application).          Column 13, lines 1-2 (p.24, lines 8-10 of the application).          Column 14, lines 13-17 (p.26, lines 15-19 of the application).</p>

*no delay or delay adjacent of the delay in the application*

Additionally, for the purposes of interference, three additional counts are proposed and illustrated in Table 2 as follows. In Column I are the counts and the claims which correspond to the count. Column II are the locations in the '027 patent. While Column III are locations in U.S. Patent Number 6,011,259, (followed by the location in the Spec. of the pending application in parenthesis), which shows conflicting subject matter relating to the elements of the claims.

Count 2	U.S. Patent No. 6,285,027	Pending U.S. Application NO. 09/901,428
<p>66. An Apparatus for analyzing chemical species comprising:</p> <p>(a) at least one vacuum pumping stage;</p> <p>(b) an ion source for producing ions from a sample substance;</p> <p>(c) at least one multipole ion guide located in at least one of said vacuum pumping stages;</p> <p>(d) a Time-Of-Flight mass to charge analyzer;</p> <p>(e) means for delivering said ions from said ion source to at least one multipole-ion guide;</p> <p>(f) means for applying electrical potentials to at least one multipole ion guide to select parent ions from said ions having a desired mass to charge ratio.</p> <p>(g) means for applying electrical potentials to at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions;</p> <p>(h) means to trap said fragment ions and any remaining said parent ions in said at least one multipole ion guide;</p> <p>(i) means to periodically release pulses of said trapped ions into said Time-Of-Flight mass to charge analyzer to detect said fragment ions with a second mass to charge ratio;</p> <p>(j) means for providing a delay between the release of the said pulses of said trapped ions and initiation of pulses in the Time-of-Flight mass to charge analyzer; and</p> <p>(k) means to adjust the delay to improve the duty cycle efficiency of said fragment ions with said second mass to charge ratio.</p>	<p>(a) Column 5, line 47: "It is to be noted that the various chambers of the device are, in known manner, connected to suitable pumps, with pump connections [being indicated at 24, 25, and 26], for the TOP instrument."</p> <p>(b) Column 5, line 24: "The instrument includes an electrospray source [10], although it is understood that any suitable ion source can be provided."</p> <p>(c) Column 5, line 32: "Downstream, there is a further chamber 18, containing an interior, subsidiary chamber 20."</p> <p>(d-e) Column 4, line 29: "periodically releasing pulses to the trapped ions into a time of flight instrument to detect ions with a second mass-to-charge ratio."</p> <p>(f) Column 4, line 21: "passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass-to-charge ratio."</p> <p>(g) Column 4, line 24: "subjecting the parent ions to collision-induced dissociation," to generate fragment ions."</p> <p>(h) Column 4, line 29: "periodically releasing pulses of the trapped ions into a time of flight instrument to detect ions with a second mass-to-charge ratio."</p> <p>(i, j) and (k) Column 4, line 32: "providing a delay between the release of the pulses of trapped ions and initiation of push-pull pulses in time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio."</p>	<p>(a) Column 11, lines 36-41 (p.21, lines 12-15). Column 11, line 67 - column 12, line 2 (p.21, lines 7-11). (b) Column 10, lines 36-40 (p.19, lines 10-12). Column 14, lines 6-14 (p.20, lines 14-19). (c) Column 11, lines 47-48 (p.21, lines 20-21). (d) Column 8, lines 8-11 (p.14, lines 8-9). (e) Column 11, lines 12-24 (p.20, lines 19-p.21, lines 1-4). Column 14, lines 38-46 (p.27, lines 12-17). Column 8, lines 40-43 (p.15, lines 7-10). Column 8, lines 51-55 (p.15, lines 14-17). Column 8, lines 64-Column 9, line 1 (p.15, line 21 - p.16, line 1). (f) Column 8, lines 64-Column 9, line 1 (p.15, line 21-p.16, line 1); Column 9, lines 19-33 (p.16, lines 15-p.17, line 2). (g) Column 8 lines 64-67 through Column 9, lines 1-3 (p.16, lines 1-5); Column 8, lines 24-35; (p.14, lines 18-p.15, line 4); Column 13, lines 3-5 (p.24, lines 11-12). (i) Column 9, lines 6-9 (p.16, lines 7-9); Column 8, lines 24-35 (p.14, lines 18-p.15, line 4); Column 13, lines 1-5 (p.24, lines 8-12). (j) Column 13, lines 1-2 (p.24, lines 8-10). Figure 6, Column 7, lines 59-60 (p.13, lines 21-23); Column 8, lines 4-6 (p.14, lines 5-7); Column 8, lines 16-18 (p.14, lines 12-14). (k) Column 13, lines 1-2 (p.24, lines 8-10). Column 14, lines 26-39 (p.27, lines 3-10). Column 12, lines 26-29 (p.23, lines 3-5); Column 7, lines 16-18 (p.12, lines 16-18); Column 3, lines 9-11 (p.4, lines 14-16); Figure 6; Column 7, lines 59-60 (p.13, lines 22-23); Column 8, lines 4-6 (p.14, lines 5-7). Column 8, lines 16-18 (p.14, lines 12-14).</p>

Counts 3	U.S. Patent No. 6,285,027	Pending U.S. Application NO. 09/901,428
<p>115. An apparatus for analyzing chemical species comprising:</p> <p>(a) at least one vacuum pumping stage;</p> <p>(b) an ion source for producing ions from a sample substance;</p> <p>(c) at least two multipole ion guides located in at least one of said vacuum pumping stages;</p> <p>(d) a Time-of-Flight mass to charge analyzer;</p> <p>(e) means for delivering said ions from said ion source into at least one multipole ion guide;</p> <p>(f) means for applying electrical potentials to a first multipole ion guide to select at least one range of mass to charge values or parent ions; and</p> <p>(g) means for applying electrical potentials to at least one multipole ion guide to subject said parent ions to collision induced dissociation to generate fragment ions in a second multipole ion guide.</p>	<p>As stated in column 4, lines 21 through 37: "(1) passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass-to-charge ratio; (2) subjecting the parent ions to collision-induced dissociation to generate fragment ions; (3) trapping the fragment ions and any remaining parent ions; (4) periodically releasing pulses of trapped ions into a time of flight instrument, and adjusting the delay between the release of the pulses of trapped ions and initiation of push-pull pulses in the time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio."</p>	<p>(a) Column 8, lines 55-57 (p. 15, lines 17-19 of the application)</p> <p>(b) Column 8, lines 1-6 (p. 14, lines 4-5); Column 8, lines 60-61 (p. 15, lines 21-22).</p> <p>(c) Column 2, lines 50-54 (p. 3, lines 21-23 - p. 4, line 1); Column 9, lines 1-9 (p. 16, lines 4-9).</p> <p>(d) Column 8, lines 31-35 (p. 15, lines 1-4); Column 9, lines 7-9 (p. 16, lines 7-9).</p> <p>(e) Column 7, lines 36-41 (p. 13 lines 5-12); Column 12, lines 10-14 (p. 22, lines 18-19); Column 13, lines 1-2 (p. 24, lines 8-10); Column 14, lines 13-17 (p. 26, lines 15-19).</p> <p>Support in Spec. of incorporated U.S. Patent Number 5,689,111: Column 2, lines 45-48; Figure 6; Column 7, lines 59-62; Column 8, lines 4-6 and lines 16-18; The Trappulse timing delay sequence shown in Figure 6 is described from column 7 line 59 through Column 8, line 42. (Note that Figure 2c of the '027 patent copies Figure 6 of the '111 patent).</p>
Count 4	U.S. Patent No. 6,285,027	Pending U.S. Application NO. 09/901,428
<p>99. A method of effecting mass analysis on an ion stream, the method comprising:</p> <p>(a) passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass to charge ratio;</p> <p>(b) subjecting the parent ions to collision induced dissociation to generate fragment ions;</p> <p>(c) trapping the fragment ions and any remaining parent ions;</p> <p>(d) periodically releasing pulses of the trapped ions into a Time-Of-Flight instrument to detect ions with a second mass to charge ratio;</p> <p>(e) providing a delay between the release of the pulses of trapped ions and initiation of pulses in the Time-Of-Flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass to charge ratio.</p>	<p>(a) Column 4, line 21: "passing the ion stream through a first mass resolving spectrometer, to select parent ions having a first desired mass-to-charge ratio."</p> <p>(b) Column 4, line 24: "subjecting the parent ions to collision-induced dissociation."</p> <p>(c-e) Column 4, line 29: "periodically releasing pulses to the trapped ions into a time of flight instrument to detect ions with a second mass-to-charge ratio."</p>	<p>(a) As stated in column 8, line 35-57 (p. 15, lines 17-19).</p> <p>(b) Column 8, lines 1-6 (p. 14, lines 4-7 of the application); Column 8, lines 60-61 (p. 15, lines 21-22).</p> <p>(c) Column 2, lines 50-54 (p. 3, lines 21-23 - p. 4, line 1); Column 9, lines 1-9 (p. 16, lines 4-9).</p> <p>(d) Column 8, lines 31-35 (p. 15, lines 1-4); Column 9, lines 7-9 (p. 16, lines 7-9).</p> <p>(e) Column 7, lines 36-41 (p. 13 lines 5-12); Column 12, lines 10-14 (p. 22, lines 18-19); Column 13, lines 1-2 (p. 24, lines 8-10); Column 14, lines 13-17 (p. 26, lines 15-19).</p> <p>Support in Spec. of incorporated U.S. Patent Number 5,689,111: Column 2, lines 45-48; Figure 6; Column 7, lines 59-62; Column 8, lines 4-6 and lines 16-18; The Trappulse timing delay sequence shown in Figure 6 is described from column 7 line 59 through Column 8, line 42. (Note that Figure 2c of the '027 patent copies Figure 6 of the '111 patent).</p>

- (5) Applying the terms of any application claim,
- (i) Identified as corresponding to the count, and
  - (ii) Not previously in the application to the disclosure of the application.

The only such term to which this might apply is the term "push-pull pulses" found in claim 115, which is a copy of claim 1 of the '027 patent. The term "pulse" is used for ion populations accelerated into the TOF mass to charge analyzer. As described above in the detailed analysis of the specification as applied to the counts, these two terms are substantially the same based on the descriptions in the pending application and the '027 specification.

**PORTION OF THIS AMENDMENT RESPONSIVE  
TO THE OFFICIAL ACTION OF JUNE 11, 2002**

Continuing on with this Amendment, claims 33 and 57 have been amended. Claims 40, 54 and 55 have been cancelled in favor of the newly added claims.

Claims 33-39, 41-43 and 56-66 were rejected under 35 USC 103(a) as being unpatentable over EP 529,885, Douglas '736, Vestal '533, Sakairi '560 and Schwartz '022.

Claims 33 and 57 have been amended to recite that only a portion of the trapped ions are pulsed from the trap. The Examiner stated in the rejection that Douglas '736 and EP 529,885 include a time of flight spectrometer located in one of the vacuum stages. The undersigned is unable to find any such reference in such prior art. EP '885 describes using a three dimensional ion trap as a mass analyzer, and Douglas describes using a quadrapole mass analyzer. Neither patent mentions or describes incorporating or using a TOF mass analyzer.

EP '885 does describe trapping of ions in an ion guide from a continuous ion beam and releasing the entire trapped population of ions into a three dimensional ion trap. None of the other cited references in any way show, suggest or disclose such traps. Further, claims 33 and 57 have been amended to recite that the pulsing is a



pulsing of a portion of the trapped ions. In a sense, EP '885 does not "pulse" ions, but merely empties all ions from its trap. The amendment to claims 33 and 57 intends to highlight the difference between pulsing and emptying by stating that only a portion of the trapped ions are pulsed.

Additionally, claim 57 recites that the ion population contains fragment ions. Neither EP '885 or Douglas '736 describe accelerating ions into an ion guide or accelerating ions from one ion guide to a second to cause ion fragmentation combined with pulsing of ions into a mass analyzer. Neither Vestal '533, Sakairi '560 or Schwartz '022 describe fragmentation of ions by accelerating ions into an ion guide or from one ion guide into a second ion guide combined with pulsing of ions into a mass analyzer. Neither Vestal '533, Sakairi '560 or Douglas '736 describe or mention in any way the trapping of ions in an ion guide.

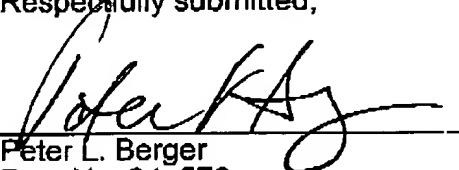
### CONCLUSION

In view of the above action and comments, it is respectfully requested that an interference be declared between this application and the '027 patent under 37 CFR 1.607.

Further, the amendments to the previously pending claims and the newly submitted claims are all believed patentable over all prior art.

Respectfully submitted,

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**AMENDED CLAIMS MARKED UP TO SHOW ALL THE CHANGES**

33. (Amended) An apparatus for analyzing chemical species comprising:

- (a) at least one vacuum pumping stage;
- (b) an ion source for producing ions from a sample substance;
- (c) at least one multipole ion guide located in at least one of said vacuum pumping stages;
- (d) a mass analyzer;
- (e) means for delivering ions from said ion source into said at least one multipole ion guide;
- (f) means for applying voltages to said at least one multipole ion guide to direct said ions along a desired ion trajectory within said at least one multipole ion guide;
- (g) means for applying additional voltages which impart energy to said ions within said at least one multipole ion guide so as to cause fragmentation of said ions located within said multipole ion guide;
- (h) means to trap ions within said at least one multipole ion guide; and
- ~~[(g)]~~ (i) means to pulse a portion of said trapped ions into said mass analyzer.

57. (Amended) A method of analyzing chemical species utilizing an ion source, a vacuum system with at least one vacuum pumping stage, at least one multipole ion guide located in at least one of said vacuum pumping stages, and a mass analyzer, said method comprising:

- (a) producing ions from a sample substance using said ion source;
- (b) directing said ions into said multipole ion guide;
- (c) fragmenting ions in said multipole ion guide to form an ion population in said multipole ion guide which contains fragment ions;
- (d) trapping said fragment ions;

[(d)] (e) pulsing a portion of said ion population which contains fragment ions toward said mass analyzer; and

[(e)] (f) conducting mass to charge analysis of at least a portion of said ion population with said mass analyzer.